

### Successful rapid intravenous desensitization for radioiodine contrast allergy in a patient requiring urgent coronary angiography

Sumeet Gandhi, MD<sup>a,\*</sup>, Dhanjit Litt, MD<sup>a,\*</sup>,  
Mark Chandy, MD, PhD<sup>b</sup>, Bao M. Nguyen, BScPhm<sup>c</sup>,  
Nina Lakhani Jindal, MD<sup>d</sup>, Susan M. Tarlo, MBBS, FRCPC<sup>e</sup>,  
and Christopher B. Overgaard, MD, MSc, FRCPC<sup>f</sup>

#### Clinical Implication

- A rapid radiographic contrast media desensitization protocol allowed a patient with a history of repeated severe non-IgE-mediated anaphylactic reactions to radiographic contrast media, in spite of standard premedication prophylaxis, to tolerate urgently needed angiography and percutaneous coronary intervention.

#### TO THE EDITOR:

An 81-year-old white woman presented to our hospital with chest pain on a background history of recurrent left main coronary artery in-stent restenosis and severe allergic reaction to iodixanol (Visipaque; GE Healthcare, Mississauga, Ontario, Canada) radiocontrast media (RCM). The patient's cardiovascular risk factors included only dyslipidemia. The patient's cardiac history was significant for prior coronary artery bypass graft surgery, severe aortic stenosis that necessitated transapical aortic valve replacement, and dual-chamber pacemaker insertion for symptomatic sinus pauses. Despite these surgical interventions, ongoing angina necessitated multiple previous percutaneous coronary intervention (PCI) procedures to the left main coronary artery. In-stent restenosis of the left main coronary artery led to multiple presentations to the hospital, where the patient's left main coronary artery was treated with a drug-eluting stent implantation and subsequent interventions that used cutting balloons and drug-eluting balloons. Other comorbidities included a childhood history of asthma, obstructive sleep apnea, gastroesophageal reflux disease, and neuropathy secondary to prior surgeries.

With each successive angiography and PCI, the patient developed an anaphylactoid reaction to Visipaque RCM, which progressed in severity. In 2008, after coronary angiography, our patient developed flushing, hypotension, and a rash consistent with hives. Subsequently, she was pretreated according to hospital protocol with diphenhydramine 50 mg orally 1 hour before and prednisone 100 mg orally 13 hours, 7 hours, and 1 hour before future angiography. In August 2012, the patient presented to the hospital with persistent chest pain and underwent coronary angiography. She was pretreated for contrast allergy as previously described. Upon initial injection of RCM while attempting to intubate the left main coronary artery, our patient's blood pressure dropped to 65/30 mm Hg, and she required intravenous fluids, hydrocortisone, epinephrine, emergent intubation, and intra-aortic balloon pump insertion. Balloon angioplasty to the left main coronary artery was

successful for critical left main coronary artery in-stent restenosis. After several days in the coronary intensive care unit, the patient was successfully extubated and ultimately discharged home.

In December 2012, recurrent chest pain prompted another attempt at coronary angiography. Pretreatment with prednisone 50 mg orally for 3 days as well as our routine hospital protocol for contrast allergy had no effect. The injection of 2 mL Visipaque RCM caused immediate hypotension and flushing, and the procedure was aborted. After the procedure, our patient was transferred to the coronary care unit for fluid resuscitation.

Our patient was identified as high risk for receiving RCM, with risk factors of a previous reaction, asthma, and cardiovascular disease. Upon consultation with allergy and immunology department personnel, a rapid intravenous desensitization protocol to Visipaque RCM was devised due to the urgency of the procedure. Before angiography, the  $\beta$ -blocker was stopped to prevent hypotension and an angiotensin-converting-enzyme inhibitor was stopped so to reduce the risk of angioedema. The pretreatment regimen was augmented for desensitization, which included the following: prednisone 100 mg (1 mg/kg) at 13 hours, 7 hours, and 1 hour before; diphenhydramine 50 mg intramuscular 1 hour before; and ranitidine 300 mg orally 1 hour before the initiation of intravenous desensitization. The desensitization protocol was initiated 2 hours before angiography, as previously described,<sup>1</sup> with Visipaque RCM (Table I). Upon completion of desensitization, there were no symptoms or signs of an anaphylactic and/or anaphylactoid response. Coronary angiography was completed with 300 mL Visipaque RCM, with complete hemodynamic stability throughout the procedure. After angiography, our patient was stable, without signs of anaphylaxis, and was discharged home in good condition.

#### DISCUSSION

The introduction of modern radioiodine contrast agents has decreased the risk of adverse reactions substantially. However, the risk of severe adverse reactions still remains measurable, with related deaths occurring in up to 1 per 100,000 administrations.<sup>2,3</sup> Adverse reactions to RCM can be classified as chemotoxic or non-IgE-mediated anaphylaxis (previously known as anaphylactoid). Chemotoxic reactions include nephrotoxicity and neurotoxicity; such reactions are concentration-dependent and are related to a chemical moiety of the contrast agent. Non-IgE-mediated anaphylactic reactions are less predictable. These are immediate hypersensitivity reactions mediated by the release of histamine from mast cells and basophils as well as complement activation. Unlike IgE-mediated anaphylactic reactions, non-IgE-mediated anaphylaxis does not involve the cross-linking of IgE antibodies. For patients with previous non-IgE anaphylactic reactions to RCM, pretreatment regimens that involve corticosteroids and antihistamines have been shown to be effective.<sup>4</sup> Unfortunately, despite adequate premedication, breakthrough reactions do occur, and there is no consensus on how to proceed when encountering patients who have had breakthrough reactions to contrast media.

The alternative RCM at our institution was iohexol (Omnipaque; GE Healthcare). This agent is hyperosmolar to Visipaque and historically has an adverse effect profile in regard to

**TABLE I.** Visipaque contrast desensitization

Dose no.	Dilution	Concentration (mg/mL)	Dose (mg)	Volume to administer (mL)	Time of administration (min)
1	1:1000	0.32	1.6	5	0
2	1:500	0.625	3.2	5	10
3	1:250	1.25	6.4	5	20
4	1:125	2.5	12.8	5	30
5	1:62.5	5	25.6	5	40
6	1:32	10	51.2	5	50
7	1:16	20	102.4	5	60
8	1:8	40	204.8	5	70
9	1:4	80	409.6	5	80
10	1:2	160	819.2	5	90
11*	1:1	320	1638.4	5	100

\*Coronary angiography proceeded after dose 11, with a total of 300 mL of Visipaque radiopaque media.

anaphylactoid reactions. We considered the use of gadolinium as an alternative to iodinated contrast; however, gadolinium generates poor imaging quality and is associated with nephrotoxicity at the dose that would be required for a successful PCI procedure. We believed that the best way to safely proceed was with contrast-enhanced coronary angiography by using rapid intravenous desensitization as previously described in the literature.<sup>1</sup> Drug desensitization is a form of induction of immune drug tolerance by which effector cells are rendered less reactive or nonreactive to IgE-mediated immune responses by rapid administration of incremental dose of an allergic substance.<sup>5</sup> The mechanism of action for desensitization in non-IgE-mediated anaphylaxis may be due to slow subclinical mediator depletion or other unknown mechanisms still not fully understood. Ultimately, this protocol was successful, with no adverse reactions associated with it. A potential contributor to previous failed pretreatment may have been the absence of H2 blockers, which were included in the pretreatment for the desensitization

protocol. A rapid desensitization protocol immediately before angiography and PCI was an invaluable clinical tool that allowed us to successfully intervene for a patient with repeated severe non-IgE-mediated anaphylactic reaction to a modern contrast agent, with failure of previous standard premedication prophylaxis.

<sup>a</sup>Division of Internal Medicine, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

<sup>b</sup>Division of Cardiology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

<sup>c</sup>Department of Pharmacy, University Health Network, Toronto, Ontario, Canada

<sup>d</sup>Division of Clinical Immunology and Allergy, Department of Medicine, University of Toronto, Toronto, Ontario, Canada

<sup>e</sup>Respiratory Division, Department of Medicine, University Health Network, University of Toronto, Toronto, Ontario, Canada

<sup>f</sup>Peter Munk Cardiac Centre, University Health Network, University of Toronto, Toronto, Ontario, Canada

\*Co-first authors.

No funding was received for this work.

The authors declare that they have no relevant conflicts of interest.

Received for publication May 2, 2013; revised June 24, 2013; accepted for publication June 28, 2013.

Available online September 9, 2013.

Corresponding author: Sumeet Gandhi, MD, University Health Network, Toronto General Hospital, 6 Eaton North Room 232, 200 Elizabeth St, Toronto ON M5G 2C4, Canada. E-mail: [sumeet.gandhi@mail.utoronto.ca](mailto:sumeet.gandhi@mail.utoronto.ca).

2213-2198/\$36.00

© 2013 American Academy of Allergy, Asthma & Immunology

<http://dx.doi.org/10.1016/j.jaip.2013.06.016>

## REFERENCES

- Hong SJ, Bloch KJ, Wong JT. Rapid IV challenge/desensitization using iso-osmolar radiopaque contrast medium (RCM) in two patients at high risk for anaphylactoid reactions. *J Allergy Clin Immunol* 2002;109:S150.
- Wang CL, Cohan RH, Ellis JH, Caoili EM, Wang G, Francis IR. Frequency, outcome, and appropriateness of treatment of nonionic iodinated contrast media reactions. *AJR Am J Roentgenol* 2008;191:409-15.
- Hunt CH, Hartman RP, Hesley GK. Frequency and severity of adverse effects of iodinated and gadolinium contrast materials: retrospective review of 456,930 doses. *AJR Am J Roentgenol* 2009;193:1124-7.
- Davenport MS, Cohan RH, Caoili EM, Ellis JH. Repeat contrast medium reactions in premedicated patients: frequency and severity. *Radiology* 2009;253:372-9.
- Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol* 2010;105:259-73.